



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Hans-Michael EGGENWEILER et al.

Examiner: San Ming R. Hui

Serial No.: 10/750,878

Group Art Unit: 1617

Filed: January 5, 2004

Title: IMIDAZOLE DERIVATIVES AS PHOSPHODIESTRASE VII INHIBITORS

REPLY BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The only issue for consideration in this appeal is the enablement rejections under 35 U.S.C. §112.

It is respectfully submitted that the legal standard of enablement continues to be misapplied in the Examiner's answer. The court mandated standard requires a three-step analysis. First, one must ask whether, an applicant's specification provides "objective enablement"? If so, then the burden of going forth shifts to the PTO, to provide reasons or evidence to doubt objective enablement. If the PTO provides such reasons or evidence, then the burden of going forth shifts to the applicant. The applicant can then establish enablement by showing that one of ordinary skill can make and use the invention with mere routine

experimentation. See *In re Marzocchi*, cited in appellants' brief. The PTO does not properly apply this three-step analysis, instead, blurring the stages.

Objective enablement is clearly provided in the specification, e.g., at page 2, lines 11 - 31 of the appellants' specification, where it is taught that the compounds of formula I inhibit PDE VII, and this statement is supported with a discussion of the methods used to determine this activity in the subject compounds. At page 3, lines 8 - 22 of the specification, it is taught that the compounds show an antagonistic effect on the production of TNF alpha, and thus are useful to treat all immune diseases, including, *for example*, rheumatoid arthritis, multiple sclerosis, Crohn's disease, diabetes, ulcerative colitis, transplant rejection reactions, cachexia and sepsis. At page 3, lines 30 - 33, it is taught that PDE VII inhibitors may also inhibit the growth of tumor cells and "are therefore suitable" for tumor therapy analogously to PDE IV inhibitors. "Objective enablement" is simply a statement that the invention has a given utility, and can be made and used as stated. The Answer never clearly addresses this phase of the analysis, instead arguing a subsequent stage in the analysis, undue experimentation. However, it is clear that "objective" enablement has been provided.

Thus, the burden shifts to the PTO to provide, "reasons or evidence" to doubt the objective enablement. A careful reading of the Answer fails to find such reasons or evidence sufficient to shift the burden back to appellants. For example, at page 15, it is argued that "reasons or evidence" constitute the argued existence of undue experimentation. Yet *Marzocchi* clearly states that this stage is not even reached before reasons or evidence are provided. Moreover, the Answer appears to argue that the breadth of the method claims itself is reason to doubt the objective enablement. However, the *Marzocchi* court clearly stated the mere *breadth* of the claims does not, without more, result in non-enablement. As the court stated,

Turning specifically to the objections noted by the Board as indicated above, it appears that these comments indicate nothing more than a concern over the *breadth* of the disputed term. If we are correct, then the relevance of this concern escapes us. It has never been contended that Applicants, when they included the disputed terms in their specification, intended only to indicate a single compound. Accepting, therefore, that the term is a generic one, its recitation must be taken as an assertion by Applicants that all of the 'considerable number of compounds' which are included in the generic term would, as a class, be operative to produce the asserted enhancement of adhesion characteristics. The only relevant concern of the patent office under these circumstances should be over the *truth* of any such assertion. The first paragraph of §112 requires nothing more than *objective enablement*. How such a teaching is set forth, either by the use of illustrative examples or by broad term analogy, it is of no importance.

Further, in this regard, it is important to note, as a matter of law, that it is not necessary for Appellants' *method* claims to exclude inoperative embodiments, inasmuch as the claims are interpreted in light of the level of understanding one of ordinary skill in the art and, for methods, are interpreted to be *per se* functional. See *In re Angstadt*, 537 F.2d 498, 190 U.S.P.Q. 214 (CCPA 1976) and *In re Dinh-Nguyen*, 492 F. 2d 856, 181 U.S.P.Q. 46 (CCPA 1974). These cases state that, for method claims, inoperative embodiments are not encompassed therein. Moreover, anti-tumor utilities are no longer to be considered to be "special", i.e., *per se* incredulous, by the Patent and Trademark Office. See *Ex parte Rubin*, 5 U.S.P.Q. 2d 1461 (BPAI 1987). As such, applications claiming these methods are, therefore, no more than typical method of use applications wherein the existence of reliable screening protocols correlatable with pharmaceutical activity in humans is sufficient to satisfy §112, in the absence of reasons to the contrary. Such screening protocols for determining the efficacy of the compounds in the anti-tumor utilities are set forth in the specification

where it is indicated that the details of using a given compound can be determined by routine testing using a known protocol which is correlated with human activity, again, see page 2, lines 18 - 31 and page 3, lines 30 – 34. Consequently, reasons or evidence to doubt the objective enablement are lacking, and the issue of "undue experimentation" does not come up. The discussion of *In re Wands*, taking up a substantial amount of the Office Action, does *not* provide the necessary reasons or evidence as to why utility is deficient, but instead is reached only in other circumstances.

Finally, even if the issue of undue experimentation were reached, it is clear that such undue experimentation is not required to make and use the present invention. The thrust of the detailed analysis in the Answer appears to be that undue experimentation is needed based on the breadth of the claims, and the Answer does not address appellants' discussion and rebuttal of this argument in their Brief. In fact, with respect to the nature of the invention, the *complexity* is in fact not supported by the breadth of the claim, as argued, in the Answer. In actuality, the nature of the invention is *not* complex, inasmuch as the use of PDE inhibitors to treat various indications is well established and would be well understood by one of skill in the art. With respect to autoimmune disorders noted in the Answer, in fact, the Answer recognizes that various types of autoimmune disorders *are* enabled by the present specification. There are no reasons why those indications singled out as non-enabled are selected.

With respect to the breadth of the claims, it is important to note that a determination of undue experimentation must be considered on a *compound by compound* basis. The mere fact that a claim is broad does *not* mean that it is undue experimentation is required to determine enablement of the compounds therein, if it is not undue experimentation to determine enablement for *each* compound in the scope of the claim. See, for example, *In re Colianni*, 561 F.2d 220, 195 U.S.P.Q. 150 (CCPA

1977). One of ordinary skill in the art can easily determine, with the protocols given in the specification, whether a given compound has the utility stated. Thus, the mere fact that many compounds must be tested is not dispositive of a lack of utility.

With respect to the guidance given by the instant specification, is submitted that the guidance is adequate. Inasmuch as pharmaceutical formulation information is given, one of ordinary skill in the art can clearly prepare the compounds for administration; dosages are given and the pharmaceutical art is well developed and administration of a compound for a given indication is quite routine. The discussion in the Answer appears to be speculation on the part of the PTO that mechanisms are not well understood, however, elucidation of a mechanism is *not* necessary, where sufficient instruction is given to administer the compounds to produce the desired effect. Thus, it is submitted that this is also a non-issue.

With respect to working examples, it is well established that working examples are *not* required to provide enablement. See, for example, *In re Borkowski*, 422 F.2d 904, 164 U.S.P.Q. 642 (CCPA 1970).

With respect to the state of the art, PDE inhibitors are well known to be implicated in signaling pathways which are instrumental in the formation of tumors. Thus, it is again not seen that this is an issue. With respect to the quantity of invention necessary, this has been discussed previously. It is maintained that the fact that a claim may be broad does not, in and of itself, result in undue experimentation, if the testing of, for example, each type of cancer or each autoimmune disorder is routine. Thus, this is not seen to be basis for lack of enablement.

Accordingly, the only rebuttal to Appellants' discussion in the prior reply is that found at page

17 of the Answer, where it is alleged that Carter provides evidence of undue experimentation. Appellants do not "misunderstand" or "mischaracterize" the reason Carter is cited. Carter is alleged to teach that no one drug can treat all tumors. The cited pages of the Carter textbook disclose various drug-tumor "interactions". They appear to suggest that some drugs do not "interact" with tumors located in the various areas listed, while others do. There is no explanation of this "interaction" and whether its significance translates to therapeutic modalities. There is no indication of the methodology used to determine the "interaction", and it is far from evident from Carter that even the "lack of interaction" translates to a *lack of therapeutic utility*. Moreover, even if Carter did stand for the proposition for which it is advanced, how does that translate to reasons or evidence why the presently claimed compounds are not effective as stated? The drugs listed in the text all differ from those employed in the present claims.

Thus, Carter falls far short of a teaching that there is no one class of compounds that would work for all tumors. Carter moreover is deficient in allowing broad conclusions to be drawn, much less conclusions respecting the presently claimed methods and compounds, in view of the deficiencies discussed above. As discussed at length in the Brief, the question is whether one of ordinary skill in art could routinely make and test *each* compound, for a given utility, in order ascertain whether a given compound is operative in the claimed method. It is again stressed that, in view of the screening tests given in the specification such a determination involves no more than routine skill and, thus, does not constitute undue experimentation.

Again, it is stressed that the legal standard does not take into account the breadth of the claim,

nor the number compounds and methods which must be tested, so long as each individual test is routine.

In conclusion, the Answer fails to properly apply the Marzocchi test and analysis, and it is maintained that ample basis to overturn the rejection remains, and the same is respectfully submitted.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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